Diabetes mellitus (See also Chap. 319) Although only a minority of obese patients are diabetic, the converse is not the case. Non-insulin-dependent, or type II, diabetes comprises about 90 percent of the diabetic population in the United States, and 80 to 90 percent of type II diabetics are obese. Obesity is an important contributory factor to the diabetes in these patients, predominantly through its influences on insulin resistance. Obesity exacerbates the diabetic state, and in many cases diabetes can be ameliorated by weight reduction.

Hyperlipoproteinemia (See also Chap. 326) Most plasma cholesterol circulates in the low-density lipoprotein (LDL) fraction, and, in the fasting state, very low density lipoproteins (VLDL) contain most of the circulating triglyceride. The association between obesity and elevated LDL levels is modest at best, especially when the relationship is corrected for factors such as age. Total-body cholesterol is increased in obesity, but this is mainly accounted for by adipose tissue cholesterol stores. Cholesterol turnover may be increased, leading to increased biliary excretion of cholesterol. This may contribute to the increased incidence of gallstone formation. Obesity has a more pronounced effect on VLDL metabolism. Hypertriglyceridemia is frequent, and the degree of obesity correlates with the level of hypertriglyceridemia. The increased triglyceride levels are due to increased hepatic VLDL production with no defect in the removal of VLDL from plasma. As discussed above, plasma insulin levels are elevated, particularly in the portal venous blood. Hyperinsulinemia can promote increased hepatic VLDL synthesis and secretion. In addition, increased plasma free fatty acid (FFA) turnover exists in obesity, and FFA extraction by the liver provides an important precursor for hepatic triglyceride synthesis. Thus, the hypertriglyceridemia in obesity may be secondary to increased hepatic VLDL secretion due to hyperinsulinemia and augmented FFA availability.

MANIFESTATIONS AND COMPLICATIONS Gross obesity produces mechanical and physical stresses that aggravate or cause a number of disorders including osteoarthritis (especially of the hips) and sciatica. Varicose veins, thromboembolism, ventral and hiatal hernias, and cholelithiasis are also more common.

Hypertension In significantly obese persons, use of the standard size blood pressure cuff leads to erroneously high readings; an oversize cuff should always be used. A strong association between hypertension and obesity is observed even when accurate measurements are obtained. The mechanism by which obesity causes hypertension is uncertain, but peripheral vascular resistance is usually normal while blood volume is increased. Weight loss leads to reductions in systemic blood pressure independent of changes in sodium balance.

Hypoventilation syndrome (Pickwickian syndrome) The obesity-hypoventilation syndrome is a heterogeneous group of disorders with differing clinical manifestations. The hypersomnolence that can occur in obesity is a manifestation of nighttime sleep apnea. In these individuals, once sleep begins, upper airway obstruction leads to hypoxemia and hypercapnia, causing arousal with return of normal respiration. Many such episodes occur each night, leading to chronic sleep deprivation and daytime somnolence. The combination of the obese habitus plus sleep-induced relaxation of the pharyngeal musculature is believed to be the cause of the intermittent upper airway obstruction. Occasionally such episodes are life-threatening (causing serious cardiac arrhythmias) and require long-term tracheostomy therapy. Chronic daytime hypoventilation is usually not as severe as that occurring during sleep and may be due to abnormalities of the respiratory control centers. Patients with hypoventilation display blunted ventilatory responses to hypercapnia and hypoxia and often develop hypercapnia and hypoxemia due to decreased basal ventilation; in addition, ventilation-perfusion mismatch may result from mechanical factors. In severe cases polycythemia, pulmonary hypertension, and cor pulmonale can result. Weight reduction will reverse these abnormalities if instituted before permanent cardiac damage develops. Some obese patients with sleep apnea and hypersomnolence do not have daytime hypoventilation and have normal ventilatory responses to hypoxia and hypercapnia. Progestational agents have been used therapeutically in the obesity-hypoventilation syndrome since they stimulate the ventilatory response to hypercapnia and hypoxia in normal subjects. Medroxyprogesterone increases ventilation and improves heart failure and erythrocytosis in these patients, although obstructive sleep apnea continues.

Adrenal function Although Cushing's disease can usually be distinguished from simple obesity on clinical grounds, laboratory testing is occasionally necessary. This can lead to confusion since 24-h urinary 17-hydroxycorticoid excretion is often elevated in obesity. Less commonly, plasma cortisol levels are also increased. Corticosteroid levels are usually suppressible with dexamethasone in obesity, but occasionally suppression is incomplete, rendering the diagnosis difficult (also see Chap. 317).

Growth hormone Secretory responses of growth hormone to a variety of stimuli such as hypoglycemia, exercise, and arginine infusion are reduced, and the starvation-induced rise in plasma growth hormone levels is attenuated.

Atherosclerosis Obesity is a risk factor for the development of coronary artery disease and stroke. Most of the risk is mediated through the associated hypertension, hyperlipoproteinemia, and diabetes. Nevertheless, even when these abnormalities are factored out, an additional, smaller risk can be ascribed to obesity per se.

TREATMENT Amelioration of hyperinsulinemia, insulin resistance, diabetes, hypertension, and hyperlipidemia can occur following weight loss. These changes are significant and enduring provided the weight loss is maintained. During weight loss all adipose tissue depots diminish proportionately. Sometimes generalized loss does not produce the attractive cosmetic effects desired. Many techniques have been proposed to effect selective adipose tissue reduction over particular regions of the body, but none is effective.

Methods of weight reduction In instances where obesity is secondary, the appropriate therapy is to treat the underlying disease. Most of the time the difficult problem of primary weight reduction must be undertaken.

Diet Caloric restriction is the cornerstone of weight reduction. From the standpoint of patient and physician this is a frustrating and demanding undertaking. The basic principles are simple. If food intake is less than energy expenditure, stored calories, predominantly in the form of fat, will be consumed. In general, a deficit of 32,000 kJ (7700 kcal) leads to loss of about 1 kg fat. By estimating the patient's daily caloric needs [approximately 125 to 150 kJ (30 to 35 kcal) per kilogram of body weight], one can calculate the daily deficit necessary to achieve a given rate of weight loss.

Dietary restriction can range from total starvation to mild caloric deprivation, and these approaches will be discussed separately. Dietary recommendations are most effective when they are specific and geared to the patient's life-style. A dietitian or a similarly trained health professional should interview each patient and estimate average daily caloric intake, identify food preferences, and characterize the eating patterns. The amount of calories to be consumed on the restricted diet should be carefully explained in terms of quantities of specific foodstuffs. Frequently, the therapist must balance the degree of restriction against potential noncompliance. The more restrictive the diet, the more rapid the weight loss, but this often leads to a greater rate of nonadherence. It is preferable to design a diet with which the patient is comfortable and that produces a modest but steady weight loss.

Schemes for weight reduction have become a profitable business in the United States, and there are almost as many diets as there are therapists. Each proponent claims that the presence or absence of certain foodstuffs is desirable for more effective weight loss. However, little evidence exists to support the claim that caloric for caloric one hypocaloric diet will lead to a greater weight loss than another. The relationship between the patient and the therapist, plus patient education and encouragement, are more important to success than are the specific dietary constituents. The major virtue of "fad" diets